REMARKS

Status of the Claims

Claims 1, 3 and 5-22 are pending in the application.

Claims 3, 5-9 and 16-19 have been withdrawn from consideration.

Claims 1, 10-15 and 22 have been rejected.

By way of this amendment, claims 3, 5-9, 14 and 16-22 have been cancelled. Claim 1 has been amended and new claims 23-38 have been added.

Upon entry of this amendment, claims 1, 10-13, 15 and 23-38 will be pending.

Summary of Amendment

Claim 1 has been amended to incorporate the subject matter of claim 22 which has been canceled. In addition, claim 1 has been amended to recite a specific minimum level of technology to the native Fc amino acid sequence.

Claims 3, 5-9 and 16-21 have been canceled without prejudice as being directed to non-elected inventions.

New claims 23-38 have been added to be directed at particular embodiments.

Support for this amendment is found throughout the specification such as pages 8-10 and 13-15 of the specification as originally filed. No new matter has been added.

Enablement

Claims 1, 10-15 and 22 are rejected under 35 U.S.C. §112, first paragraph, because it is asserted that the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention for the same reasons set forth in the previous Office Action, mailed April 22, 2002. It is the examiner's position that the specification does not provide sufficient guidance and examples as to which modifications would be acceptable to retain these specific structural and functional properties of claimed antibodies to be used in the claimed method for enhancing cytotoxicity elicited by antibody *in vivo*, which method comprises disrupting activation of SHIP by FcRIIB. In addition, the term "modifying" encompass any substitution, deletion or insertion (page 14, lines 13-16 of Specification as filed) of Fc portion of the antibody that will affect their structural and functional properties. The Examiner asserts that protein chemistry is probably one of the most unpredictable areas of

biotechnology and that it is known in the art that even single amino acid changes or differences in a proteins amino acid sequence can have dramatic effects on the protein's function. Applicant respectfully disagrees.

It is well established that the requirements of §112, first paragraph, are met so long as: (1) the invention is described in the specification as broadly as it is claimed; and (2) the information provided in the specification is sufficient for persons of ordinary skill in the art having the specification before them to make and use the invention. Moreover, it is well established that in determining whether or not the specification enables the claimed invention, the Patent Office must accept the objective truth of an Applicant's assertion unless there is some basis to doubt the objective truth of the assertions. To establish a *prima facie* case of non-enablement, the examiner must provide a reasonable explanation as to why the scope of protection provided by a claim is not adequately enabled by the disclosure. *In re Wright*, 999 F.2d 1557, 1561-62, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). In determining whether or not a disclosure is enabled, Applicant refers to *In re Marzocchi*, 439 F2d. 220, 223, 169 USPQ 367, 369 (CCPA 1971) which states:

> As a matter of Patent Office practice, a specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as in compliance with the enabling requirement of the first paragraph of §112 unless there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support.

Any assertion by the Patent Office that an enabling disclosure is not commensurate in scope with the protection sought must be supported by evidence or reasoning substantiating the doubts so expressed. *In re Dinh-Nguyen*, 181 U.S.P.Q. 46 (C.C.P.A. 1974); *In re Bowen*, 181 U.S.P.Q. 48 (C.C.P.A. 1974).

In the present case, it is the examiner's position that the specification does not set forth sufficient guidance and teachings to enable how to make and/or use. It is asserted that the art is unpredictability and that one skilled in the art could not practice the invention without undue experimentation.

The question of undue experimentation is a matter of degree. The fact that some experimentation is necessary does not preclude enablement; what is required is that the amount

of experimentation "must not be unduly extensive". *Atlas Powder Co., v. E.I. DuPont De Nemours & Co.*, 750 F2d 1569, 1576, 224 USPQ 409, 413 (Fed. Cir. 1984). The Patent and Trademark Office Board of appeals addressed this when it stated:

> The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the invention claimed.

Ex parte Jackson, 217 USPQ 804, 807 (1982).

Claim 1 has been amended to recite that the therapeutic antibody whose cytotoxicity is enhanced by the present invention retains or has enhanced binding to activating Fc receptors and that the Fc region of the antibody is at least 80% homologous with a native Fc region.

Applicant has amended claim 1 to refer to both homology to the native Fc sequence as well as functional limitations (the claim recites that the antibody is a therapeutic antibody, wherein the modified Fc region retains binding to activating receptors. New claims 23 and 24 further limit the percent homology to 90 and 95% respectively. New claims 25-29 further limit the claims with respect to amino acid substitutions. New claim 30-34 further limit the claims with respect to amino acid additions. New claim 33 and 34 further limit the claims with respect to amino acid deletions.

As amended, the claims variously recite limitations on the structural changes made to the therapeutic antibody and specific functions which the final product possesses. One skilled in the art could produce molecules according to the invention without undue experimentation.

The claims are in compliance with the enablement requirement of the first paragraph of section 112. Applicant respectfully requests that the rejection of claims 1, 10-15 and 22 under 35 U.S.C. §112, first paragraph, because it is asserted that the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention, be withdrawn.

Written Description

Claims 1, 10-15 and 22 are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably

convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for the same reasons set for the in the previous Office Action, mailed April 22, 2002.

It is asserted in the Official Action that

> there is no described or art-recognized correlation or relationship between the structure of the invention, modified antibody, that reduced binding affinity for FcRIIB, due to modification of the Fc portion of the antibody, while retaining or enhancing binding to FcRIIA and Fc RIIIA that can be used in a method for enhancing cytotoxicity elicited by a this antibody *in vivo*, which method comprises disrupting activation of SHIP by Fc RIIB, the feature deemed essential to the instant invention.

Therefore, it is asserted, one of skill in the art would not, based on the instant disclosure, envisage the claimed method for enhancing cytotoxicity of an antibody, specific for a HER2/neu growth factor receptor or for CD20 B cell antigen. Applicant respectfully disagrees.

To fulfill the written description requirement of §112, first paragraph, the patent specification must clearly allow persons of ordinary skill in the art to recognize that the inventor invented what is claimed. The written description requirement of §112, first paragraph, is met so long as the invention is described in the specification as broadly as it is claimed.

The Court of Appeals for the Federal Circuit in *Regents of University of California v. Eli Lilly & Co.*, 119 F.3d 1559 (Fed. Cir. 1997), providing guidance as to what is necessary to satisfy the written description requirement when claiming a genus of DNA molecules stated:

> A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus.

119 F.3d at 1569. The Federal Circuit also addressed the issue of written description. *Enzo Biochem, Inc. v. Gen-Probe Inc.*, 296 F.3d 1316 (Fed. Cir. 2002), vacating 285 F.3d 1013 (Fed. Cir. 2002). The district court found all claims invalid on summary judgment for lack of written description, holding that the descriptions were purely functional and that the probes deposited at the ATCC did not supplement the content of the specification. The Federal Circuit reversed stating that not all functional descriptions of "genetic material" fail to meet the written

description requirement. *Enzo*, 296 F.3d at 1324. The Court referred to the PTO's Written Description Guidelines (Guidelines) on this point, holding that the written description can be satisfied if disclosed functional characteristics are coupled with a known or disclosed correlation between function and structure. *Id.* at 1325.

Applicant respectfully asserts that the claimed invention complies with the written description requirement. In the present application, the structure as claimed is clear, the function is clear and the correlation between the two is clear. Claim 1 as amended refers to an Fc region that is 80% homologous to a native Fc region. New claim 23 refers to an Fc region that is 90% homologous to a native Fc region. New claim 24 refers to an Fc region that is 95% homologous to a native Fc region. The structure of these molecules are clearly defined. Moreover, new claims 25-38 refer to Fc regions that are 80% homologous to a native Fc region and have limitations with respect to substitutions, additions or deletions. The structures are known as are the functions which are associated with Fc region including binding to the Fc receptors.

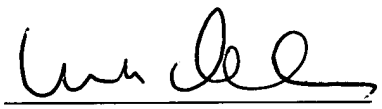
The claims are in compliance with the written description requirement of the first paragraph of section 112. Applicant respectfully requests that the rejection of claims 1, 10-15 and 22 under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention be withdrawn.

Conclusion

In view of the foregoing, Applicant submits that the claims 1, 10-13, 15 and 23-38 are in condition for allowance. An early indication of allowability and notice of allowance is earnestly solicited. Applicant invites the Examiner to contact the undersigned at 215.665.5592 to clarify any unresolved issues raised by this response.

As indicated on the transmittal accompanying this response, the Commissioner is hereby authorized to charge any debit or credit any overpayment to Deposit Account No. 50-1275.

Respectfully submitted,



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